IN THE CLAIMS

Please amend the claims as follows:

1. (Original) A system, comprising;

a sensor to sense a physiological signal indicative of a predetermined cardiac condition;

a gene regulatory signal delivery device that emits a regulatory signal which directly or indirectly regulates a regulatable transcriptional control element; and

a controller coupled to the sensor and the gene regulatory signal delivery device, the controller adapted to control the emission of the regulatory signal based on at least the sensed physiological signal.

2. (Original) The system of claim 1, wherein the gene regulatory signal delivery device comprises an electric field generator which emits an electric field.

3. (Currently Amended) The system of claim 1, wherein the gene regulatory signal delivery device comprises an ~~electric~~ electromagnetic field generator which emits an electromagnetic field having a predetermined frequency.

4. (Original) The system of claim 1, wherein the gene regulatory signal delivery device comprises a light emitter which emits a light having a predetermined wavelength and energy.

5. (Original) The system of claim 1, wherein the gene regulatory signal delivery device comprises a speaker which emits an acoustic energy.

6. (Original) The system of claim 1, wherein the gene regulatory signal delivery device comprises a drug delivery device which contains a chemical agent.

7. (Original) The system of claim 1, wherein the gene regulatory signal delivery device comprises a thermal radiator which emits a thermal energy.

8. (Original) The system of claim 1, further comprising an event detector to detect the predetermined cardiac condition from the sensed physiological signal, and wherein the controller is adapted to control the emission of the regulatory signal in response to a detection of the predetermined cardiac condition.

9. (Original) The system of claim 8, wherein the event detector comprises an event parameter generator to produce one or more condition parameters related to at least one of a type and a degree of the predetermined cardiac condition, and the controller comprises a regulatory signal parameter controller to quantitatively control the emission of the regulatory signal based the one or more condition parameters.

10. (Original) The system of claim 8, wherein the sensor comprises an electrogram sensing circuit, and the event detector comprises an arrhythmia detector.

11. (Original) The system of claim 10, wherein the event detector comprises an atrial fibrillation detector.

12. (Original) The system of claim 10, wherein the event detector comprises a ventricular fibrillation detector.

13. (Original) The system of claim 8, wherein the sensor comprises a sensor sensing an physiological signal indicative of ischemia, and the event detector comprises an ischemia detector.

14. (Original) The system of claim 8, wherein the sensor comprises a metabolic sensor adapted to sense a signal indicative of a cardiac metabolic level.

15. (Original) The system of claim 14, wherein the sensor comprises at least one of a pH sensor, an oxygen pressure (PO_2) sensor, a carbon dioxide pressure (PCO_2) sensor, a glucose sensor, a creatine sensor, a C-creative protein sensor, a creatine kinase sensor, and a creatine kinase-MB sensor.

16. (Original) The system of claim 8, wherein the sensor comprises an impedance sensor to sense tissue impedance.

17. (Original) The system of claim 16, wherein the impedance sensor comprises a pulmonary impedance sensor.

18. (Original) The system of claim 17, wherein the impedance sensor comprises a respiratory sensor.

19. (Original) The system of claim 8, wherein the sensor comprises a pressure sensor to sense a pressure in a cardiovascular system.

20. (Original) The system of claim 19, wherein the pressure sensor comprises at least one of a left atrial pressure sensor, a left ventricular pressure sensor, an artery pressure sensor, and a pulmonary arterial pressure sensor.

21. (Original) The system of claim 20, wherein the event detector comprises a systolic dysfunction detector.

22. (Original) The system of claim 20, wherein the event detector comprises a diastolic dysfunction detector.

23. (Original) The system of claim 8, wherein the sensor comprises a stroke volume sensor.

24. (Original) The system of claim 8, wherein the sensor comprises a neural activity sensor.

25. (Original) The system of claim 24, wherein the neural activity sensor comprises a neurohormone sensor to sense a neurohormone level.

26. (Original) The system of claim 24, wherein the neural activity sensor comprises a action potential recorder to sense neural electrical activities.

27. (Original) The system of claim 8, wherein the sensor comprise a heart rate variability detector.

28. (Original) The system of claim 8, wherein the sensor comprises a renal function sensor.

29. (Original) The system of claim 28, wherein the renal function sensor comprises at least one of a renal output sensor, a filtration rate sensor, and an angiotensin II level sensor.

30. (Original) The system of claim 8, wherein the sensor comprises an acoustic sensor adapted to sense at least one of heart sounds and respiratory sounds.

31. (Original) The system of claim 30, wherein the event detector to detect the predetermined cardiac condition when third hear sound (S3) amplitude exceeds a predetermined threshold.

32. (Original) A system, comprising;

an implantable medical device system including:

a sensor to sense a physiological signal indicative of a predetermined cardiac condition;

an implant telemetry module to receive an external command;

a gene regulatory signal delivery device that emits a regulatory signal which directly or indirectly regulates a regulatable transcriptional control element; and

an implant controller coupled to the event detector and the implant telemetry

module, the implant controller including a gene expression control module adapted to control the emission of the regulatory signal based on at least one of the sensed physiological signal and the external command; and

an external system including an external telemetry module to transmit the external command to the implant telemetry module.

33. (Original) The system of claim 32, wherein the gene regulatory signal delivery device comprises an electric field generator which emits an electric field.

34. (Currently Amended) The system of claim 32, wherein the gene regulatory signal delivery device comprises an ~~electric~~ electromagnetic generator which emits an electromagnetic field having a predetermined frequency.

35. (Original) The system of claim 32, wherein the gene regulatory signal delivery device comprises a light emitter which emits a light having a predetermined wavelength and energy.

36. (Original) The system of claim 32, wherein the gene regulatory signal delivery device comprises a speaker which emits an acoustic energy.

37. (Original) The system of claim 32, wherein the gene regulatory signal delivery device comprises a drug delivery device which contains a chemical agent.

38. (Original) The system of claim 32, wherein the gene regulatory signal delivery device comprises a thermal radiator which emits a thermal energy.

39. (Original) The system of claim 32, wherein the implantable medical device system further comprises an event detector to detect the predetermined cardiac condition from the sensed physiological signal, and wherein the implant controller is adapted to control the emission of the regulatory signal in response to at least one of the predetermined cardiac condition and the external command.

40. (Original) The system of claim 39, wherein the event detector comprises an event parameter generator to produce one or more condition parameters related to at least one of a type and a degree of the predetermined cardiac condition, and the implant controller comprises a regulatory signal parameter controller to quantitatively control the emission of the regulatory signal based the one or more condition parameters.

41. (Original) The system of claim 39, wherein the sensor comprises an electrogram sensing circuit, and the event detector comprises an arrhythmia detector.

42. (Original) The system of claim 41, wherein the event detector comprises an atrial fibrillation detector.

43. (Original) The system of claim 41, wherein the event detector comprises a ventricular fibrillation detector.

44. (Original) The system of claim 39, wherein the sensor comprises a sensor sensing an physiological signal indicative of ischemia, and the event detector comprises an ischemia detector.

45. (Original) The system of claim 39, wherein the sensor comprises a metabolic sensor adapted to sense a signal indicative of a cardiac metabolic level.

46. (Original) The system of claim 45, wherein the sensor comprises at least one of a pH sensor, an oxygen pressure (PO_2) sensor, a carbon dioxide pressure (PCO_2) sensor, a glucose sensor, a creatine sensor, a C-creative protein sensor, a creatine kinase sensor, and a creatine kinase-MB sensor.

47. (Original) The system of claim 39, wherein the sensor comprises an impedance sensor to sense tissue impedance.

48. (Original) The system of claim 47, wherein the impedance sensor comprises a pulmonary impedance sensor.

49. (Original) The system of claim 48, wherein the impedance sensor comprises a respiratory sensor.

50. (Original) The system of claim 39, wherein the sensor comprises a pressure sensor to sense a pressure in a cardiovascular system.

51. (Original) The system of claim 50, wherein the pressure sensor comprises at least one of a left atrial pressure sensor, a left ventricular pressure sensor, an artery pressure sensor, and a pulmonary arterial pressure sensor.

52. (Original) The system of claim 51, wherein the event detector comprises a systolic dysfunction detector.

53. (Original) The system of claim 51, wherein the event detector comprises a diastolic dysfunction detector.

54. (Original) The system of claim 39, wherein the sensor comprises a stroke volume sensor.

55. (Original) The system of claim 39, wherein the sensor comprises a neural activity sensor.

56. (Original) The system of claim 55, wherein the neural activity sensor comprises a neurohormone sensor to sense a neurohormone level.

57. (Original) The system of claim 55, wherein the neural activity sensor comprises a action potential recorder to sense neural electrical activities.

58. (Original) The system of claim 39, wherein the sensor comprise a heart rate variability detector.

59. (Original) The system of claim 39, wherein the sensor comprises a renal function sensor.

60. (Original) The system of claim 59, wherein the renal function sensor comprises at least one of a renal output sensor, a filtration rate sensor, and an angiotensin II level sensor.

61. (Original) The system of claim 39, wherein the sensor comprises an acoustic sensor adapted to sense at least one of heart sounds and respiratory sounds.

62. (Original) The system of claim 61, wherein the event detector to detect the predetermined cardiac condition when third hear sound (S3) amplitude or activity exceeds a predetermined threshold level.

63. (Original) The system of claim 32, wherein the implantable medical device system further comprises a pacing circuit coupled to the implant controller, and wherein the implant controller includes a pacing control module adapted to control a delivery of pacing pulses in conjunction with the emission of the regulatory signal.

64. (Original) The system of claim 63, wherein the pacing control module is further adapted to control the delivery of pacing pulses based on at least the external command.

65. (Original) The system of claim 63, wherein the implantable medical device system further comprises a cardiac resynchronization therapy (CRT) circuit coupled to the implant controller, and wherein the implant controller includes a CRT control module adapted to control a delivery of CRT in conjunction with the emission of the regulatory signal.

66. (Original) The system of claim 63, wherein the implantable medical device system further comprises a remodeling control (RCT) therapy circuit coupled to the implant controller, and wherein the implant controller includes a RCT therapy control module adapted to control a delivery of RCT therapy in conjunction with the emission of the regulatory signal.

67. (Original) The system of claim 63, wherein the implantable medical device system further comprises a defibrillation circuit coupled to the implant controller, and wherein the implant controller includes a defibrillation control module adapted to control a delivery of cardioversion/defibrillation shocks in conjunction with the emission of the regulatory signal.

68. (Original) The system of claim 67, wherein the defibrillation control module is further adapted to control the delivery of cardioversion/defibrillation shocks based on at least the external command.

69. (Original) The system of claim 67, further comprising at least one atrial defibrillation lead coupled to the defibrillation circuit to deliver the defibrillation shocks to one or more atria, and wherein the defibrillation control module comprises an atrial defibrillation control module.

70. (Original) The system of claim 67, further comprising at least one ventricular defibrillation lead coupled to the defibrillation circuit to deliver the defibrillation shocks to one or more ventricles, and wherein the defibrillation control module comprises a ventricular defibrillation control module.

71. (Original) The system of claim 32, wherein the implantable medical device system comprises a hermetically sealed can to house at least the implant controller and the implant telemetry module.

72. (Original) The system of claim 71, wherein the hermetically sealed can further houses the sensor.

73. (Original) The system of claim 72, wherein the sensor is external to the hermetically sealed can.

74. (Original) The system of claim 32, wherein the external system comprises:

a presentation device to present the sensed physiological signal; and

a user input device to receive the external command.

75. (Original) The system of claim 74, wherein the external system comprises a programmer.

76. (Original) The system of claim 74, wherein the external system comprises an advanced patient management system including:

an external device wirelessly coupled to the implantable medical device system via telemetry;

a remote device to provide for access to the implantable medical device system from a distant location; and

a network connecting the external device and the remote device.

77. (Original) The system of claim 76, wherein the external device comprises the user input.

78. (Original) The system of claim 76, wherein the remote device comprises the user input.

79. (Original) A method, comprising:

sensing a physiological signal indicative of a predetermined cardiac condition;

detecting the predetermined cardiac condition from the physiological signal; and

delivering a regulatory signal which directly or indirectly regulates expression from a regulatable transcriptional control element in response to at least the detection of the predetermined cardiac condition.

80. (Original) The method of claim 79, wherein sensing the physiological signal comprises sensing the physiological signal with an implantable sensor.

81. (Original) The method of claim 80, further comprising receiving a command, and delivering the regulatory signal in response to the command.

82. (Original) The method of claim 80, further comprising receiving a further command, and stopping delivering the regulatory signal in response to the further command.

83. (Original) The method of claim 82, wherein receiving the command comprises receiving an external command transmitted to an implantable device from an external system.

84. (Original) The method of claim 83, further comprising:

transmitting one or more of the sensed physiological signal and a detection of the predetermined cardiac condition to an external system; and

presenting the one or more of the sensed physiological signal and a detection of the predetermined cardiac condition through the external system.

85. (Original) The method of claim 84, where receiving the external command comprises receiving the external command entered by a physician or other caregiver through the external system.

86. (Original) The method of claim 84, where receiving the external command comprises receiving the external command entered by a patient through the external system.

87. (Original) The method of claim 79, wherein the regulatory signal induces gene expression from the regulatable transcriptional control element.

88. (Original) The method of claim 79, wherein the regulatory signal decreases gene expression from the regulatable transcriptional control element.

89. (Original) The method of claim 79, wherein a magnitude of the regulatory signal delivered is proportional to the level or amount of the physiological signal.

90. (Original) The method of claim 79, wherein an electric field is delivered.

91. (Original) The method of claim 79, wherein a light having a predetermined wavelength is delivered.

92. (Original) The method of claim 79, wherein an acoustic energy is delivered.

93. (Original) The method of claim 79, wherein a chemical agent is delivered.

94. (Original) The method of claim 79, wherein thermal energy is delivered.

95. (Original) The method of claim 79, wherein the sensing the physiological signal comprises sensing at least one electrogram, and detecting the predetermined cardiac condition comprises detecting an arrhythmia.

96. (Original) The method of claim 95, wherein detecting the predetermined cardiac condition comprises detecting an atrial fibrillation.

97. (Original) The method of claim 95, wherein detecting the predetermined cardiac condition comprises detecting a ventricular fibrillation.

98. (Original) The method of claim 79, wherein the sensing the physiological signal comprises sensing an physiological signal indicative of ischemia, and detecting the predetermined cardiac condition comprises detecting an ischemia.

99. (Original) The method of claim 79, wherein the sensing the physiological signal comprises sensing a signal indicative of a cardiac metabolic level.

100. (Original)The method of claim 99, wherein sensing the signal indicative of the cardiac metabolic level comprises sensing at least one of a pH value, an oxygen pressure (PO_2), a carbon dioxide pressure (PCO_2), a glucose level, a creatine level, a C-creative protein level, a creatine kinase level, and a creatine kinase-MB level.

101. (Original) The method of claim 79, wherein the sensing the physiological signal comprises sensing tissue impedance.

102. (Original) The method of claim 101, wherein the sensing the tissue impedance comprises sensing pulmonary impedance.

103. (Original) The method of claim 101, wherein the sensing the tissue impedance comprises sensing an impedance indicative of minute ventilation.

104. (Original) The method of claim 79, wherein the sensing the physiological signal comprises sensing a pressure in a cardiovascular system.

105. (Original) The method of claim 104, wherein the sensing the pressure comprises sensing at least one of a left atrial pressure, a left ventricular pressure, an arterial pressure, and a pulmonary arterial pressure.

106. (Original) The method of claim 104, wherein detecting the predetermined cardiac condition comprises detecting a systolic dysfunction.

107. (Original) The method of claim 104, wherein detecting the predetermined cardiac condition comprises detecting a diastolic dysfunction.

108. (Original) The method of claim 79, wherein the sensing the physiological signal comprises sensing a stroke volume.

109. (Original) The method of claim 79, wherein the sensing the physiological signal comprises sensing a neural activity.

110. (Original) The method of claim 109, wherein the sensing the neural activity comprises sensing a neurohormone level.

111. (Original) The method of claim 109, wherein the sensing the neural activity comprises sensing neural electrical activities.

112. (Original) The method of claim 111, wherein the sensing the physiological signal comprises detecting a heart rate variability.

113. (Original) The method of claim 79, wherein the sensing the physiological signal comprises sensing a renal function.

114. (Original) The method of claim 113, wherein the sensing the renal function comprises sensing at least one of a renal output, a filtration rate, and an angiotensin II level.

115. (Original) The method of claim 79, wherein the sensing the physiological signal comprises sensing at least one of heart sounds and respiratory sounds.

116. (Original) The method of claim 115, wherein detecting the predetermined cardiac condition comprises detecting a predetermined cardiac condition when third hear sound (S3) amplitude exceeds a predetermined threshold.

117. (Original) The method of claim 79, wherein detecting the predetermined cardiac condition comprises detecting a degree of the predetermined cardiac condition.

118. (Original) The method of claim 79, further comprising delivering pacing pulses in conjunction with delivering the regulatory signal.

119. (Original)The method of claim 118, further comprising delivering a cardiac resynchronization therapy (CRT) in conjunction with delivering the regulatory signal.

120. (Original) The method of claim 118, further comprising delivering a remodeling control (RCT) therapy in conjunction with delivering the regulatory signal.

121. (Original) The method of claim 118, further comprising delivering cardioversion/defibrillation shocks in conjunction with delivering the regulatory signal.

122. (Original) The method of claim 121, wherein delivering the cardioversion/defibrillation shocks comprises delivering atrial defibrillation shocks.

123. (Original) The method of claim 121, wherein delivering the cardioversion/defibrillation shocks comprises delivering ventricular defibrillation shocks.

124. (Original) A method to prepare an implantable device effective to control expression of at least one exogenously introduced expression cassette which includes a regulatable transcriptional control element operably linked to an open reading frame in an animal at risk of a cardiac condition, comprising:

introducing to an implantable medical device a gene regulatory signal

delivery device that emits a regulatory signal which directly or indirectly regulates the transcriptional control element, wherein the expression of the open reading frame in the at least one exogenously introduced expression cassette is capable of preventing, inhibiting or treating the condition or at least one symptom thereof.

125. (Original) A method to control expression of at least one exogenously introduced expression cassette which includes a regulatable transcriptional control element operably linked to an open reading frame in an animal at risk of a cardiac condition, comprising:

providing an animal comprising the system of claim 1 or 32, which animal is at risk of the cardiac condition;

introducing to the animal at least one expression cassette which includes a transcriptional control element directly or indirectly regulated by the emitted signal operably linked to an open reading frame, the expression of which is capable of preventing, inhibiting or treating the condition or at least one symptom thereof; and

directing signal emission in response to detection of the condition so as to control expression of the open reading frame.

126. (Original) A method to control expression of at least one exogenously introduced expression cassette which includes a regulatable transcriptional control element operably linked to an open reading frame in an animal at risk of a cardiac condition, comprising:

providing an animal comprising at least one exogenously introduced expression cassette which includes a transcriptional control element directly or indirectly regulated by a signal operably linked to an open reading frame, the expression of which is capable of preventing, inhibiting or treating a cardiac condition or at least one symptom thereof, which animal is at risk of the cardiac condition;

introducing to the animal the system of claim 1 or 32, wherein the emitted signal directly or indirectly regulates the transcriptional control element and thereby the expression of the open reading frame;

directing signal emission in response to detection of the condition so as to control

expression of the open reading frame.

127. (Original) The method of claim 124, 125 or 126 wherein the regulatable transcriptional control element is regulated by light, accoustic energy, an electric field, thermal energy, electromagnetic energy, or a chemical agent.

128. (Original) The method of claim 124, 125 or 126 wherein expression of the open reading frame inhibits or treats arrhythmia, atrial defibrillation, diastolic dysfunction, ventricular defibrillation, ventricular remodeling, heart failure, bradycardia, or ischemia.

129. (Original) The method of claim 125 or 126 wherein the at least one expression cassette is present in a DNA vector.

130. (Original) The method of claim 125 or 126 wherein the at least one expression cassette is present in a viral vector.

131. (Original) The method of claim 125 or 126 wherein the at least one expression cassette is introduced via intramuscular or intravenous administration.

132. (Original) The method of claim 125 or 126 wherein the at least one expression cassette is present in a plasmid vector.

133. (Original)The method of claim 125 or 126 wherein the at least one expression cassette includes a Serca2A gene.

134. (Original) The method of claim 125 or 126 wherein the at least one expression cassette includes an atrial specific ion channel protein gene.

135. (Original) The method of claim 125 or 126 wherein the at least one expression cassette encodes a gene product which regulates gap junctions.

136. (Original) The method of claim 125 or 126 wherein expression of the at least one expression cassette enhances cardiac performance in the mammal.

137. (Original) The method of claim 125 or 126 wherein the at least one expression cassette encodes a gene product that alters conduction in myocardium.

138. (Original) The method of claim 125 or 126 wherein the regulatable transcriptional control element is a promoter and the open reading frame is in antisense orientation relative to the regulatable promoter.

139. (Original) The method of claim 125 or 126 wherein the at least one expression cassette encodes a gene product which alters I_{kl}.

140. (Original) The method of claim 125 or 126 wherein the regulatable transcriptional control element is a promoter.

141. (Original) The method of claim 140 further comprising a tissue- or cell-specific enhancer.

142. (Original) The method of claim 125 or 126 wherein the regulatable transcriptional control element is an enhancer.

143. (Original) The method of claim 142 further comprising a cell- or tissue-specific promoter.

144. (Original) The method of claim 125 or 126 wherein the system is implanted in or on the heart.

145. (Original) The method of claim 125 or 126 wherein the system is implanted in or on a blood vessel.

146. (Original) The method of claim 125 or 126 wherein the open reading frame encodes a dominant negative gene product.

147. (Original) The method of claim 125 or 126 wherein at least one expression cassette encodes vascular endothelial growth factor 121 ($VEGF_{121}$), protein kinase B (AKt), catalytic subunit of human telomerase (hTERT), connexin43, fibroblast growth factor 4 (FGF-4), hypoxia-inducible transcription factor 1 alpha (HIF-1α), B cell leukemia protein 2 (Bcl-2), adenylcyclase IV (AC_{VI}), beta adenergic receptor kinase 1 (βARK-1), beta-adrenergic receptor (β-AR), vasopressin receptor 2 (V_2), sarcoplasmic reticulum $Ca2^+$ ATPase (Serca2A) or phospholamban.

148. (Original) The method of claim 125 or 126 wherein the animal is a mammal.